For your reference the claims are hereby amended as followed: (from the original application)

What is claimed is:

1-2 withdrawn

7-20 withdrawn

3. A method of treating cancer in a subject, comprising of administering a therapeutically effective amount of a positron-emitting compound to the subject, wherein the positron emitting compound comprises one or more atoms of fluorine-18 atoms such as ^{18}F-fluorodeoxyglucose.

4. The method of claim 3, wherein the positron-emitting compound is ^{18}F-2-fluoro-2-deoxyglucose

5. The method of claim 3, wherein the positron emitting compound is ^{18}F-fluorocholine.

6. The method of claim 3, wherein the positron-emitting compound is [methyl-^{11}C] choline.

For the 112 First Paragraph Rejections:

The following description will explain, in clear and precise terms as to enable any persons skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the applicant of carrying out this invention.

The synthesis of ^{18}F-2-fluro-2-deoxyglucose (FDG) follows a familiar procedure reported in the literature (Hamacher et al., J. Nucl.Mec.27, 235-238 1986 and a copy of the paper is enclosed). The ^{15}O water target is bombarded with protons in the cyclotron. In the applicant's case, it was done by a MiniTrace cyclotron manufactured by General Electrics. The resulting ^{18}F water is shunted, via a polyetheretheketone tubing to a FDG micro-laboratory module where the actual synthesis process occurs. The resulting FDG is collected in a sterile vial,

checked for quality control, and then delivered in lead shielded syringes in unit dose format for use by physicians on their patients. A copy of the standard procedures and the various methods of quality control are enclosed for the examiner's review.

Typically FDG can be purchased nowadays easily in most western countries including the United States. With a half life of 110 minutes, cyclotron centers are now being established in most major metropolitan cities for the supply of FDG for the diagnostic use of PET (Positron Emission Tomography) centers. FDG has been cleared by the FDA for human use and there has never been any serious reactions reported in its use for nearly twenty years. In essence, any person skilled in the art can order a specific dose of FDG with the local cyclotron center with a delivery service.

To carrying out the invention as stated in claims 3-6 in the treatment of disease from hereon defined specifically as cancer using positron emitting compounds such as FDG, ^{18}F-fluorocholine and methyl-^{11}C choline, a person or a physician licensed in the practice of oncology or radiotherapy in this case, has to calculate the effective dose required for these compounds to work. FDG is chosen in this respect to set as an example. The amount of radiation dose estimates for radiopharmaceuticals such as FDG per unit of mCi for different human organs have been calculated. A table composed by the Oak Ridge Institute For Science and Education is enclosed for your information.

Initially the patient has to undergo a normal PET scan to determine the staging of the disease, the amount of cancer in approximate volume and the so-called Standard Uptake Value of FDG (SUV). SUV is defined as the uptake value of FDG in the tumor over the standard of the baseline tissues of the body per unit volume. From the Oak Ridge table one can see that the effective dose equivalent (EDE) of baseline general body tissue is about 1.5 rem/15m Ci, the 15mCi being the general high limit of a diagnostic dose of FDG. For cancerous tumors, the EDE is calculated conservatively by multiplying the SUV with the EDE of general tissue for the dose of mCi of FDG given. The reason why this is a conservative calculation is because if the SUV is high, for example like over 10, then there

should be other local radiation effect from beta particles liberated from the positron carrying FDG. That means more EDE for the tumor. It has been estimated by a correspondence with V Gates of Ohio State University that a 1cm tumor with a 1% uptake of FDG can receive as much as 137.5 rems. But if one is to stay on the conservative side then the following formula will apply:

EDE of cancerous tumor = EDE of general body tissue x SUV in rems

If we simply that general body tissue will receive 0.1 rem per mCi of FDG, the formula will be

EDE of cancerous tumor = Number of mCi given x 0.1x SUV in rems

In the case of FDG, the EDE in rems will be equal to the same in cGy, so the formula can simply be applied as

EDE of cancerous tumor = 0.1 Number of mCi x SUV in cGy

In the case that we have shown here with renal cell carcinoma, a dose of 30mCi was given and the SUV is 10, then the

EDE of that renal cell carcinoma received was at least 0.1x30x10 = 30cGys

For those that want to use the invention to treat a case of cancer, the most common form of combination is with radiation therapy. So if for each fraction of radiation therapy of a standard 200cGy given and with the concurrent use of this invention for a renal cancer as illustrated, the actual delivered dose to the tumor is at least 200cGys + 30cGys (from the FDG given) = 230 Gys. The actual amount of increase which is 15% actual will have an effective radiation dose much higher than that. For the practicing radiotherapist, the actual effective dose, taken into effect of the shoulder effect of radiation and the accelerated effect of a higher dose fractionation, will be close to 20 to 30% higher for a similar course of 200cGys given for a total of 20 to 25 fractions, for example. Such an increase will be very significant and will enable an "actual curative dose" to only the cancerous part of the tumor but not to other vital organs such as the heart or major

arteries surrounding the tumor. In practice, and because of the safety of FDG (which is essentially sugar solution with positron radiation), radiotherapists can, and should, easily adopt the combination of safe doses of FDG with their daily fractions of radiation for the treatment of cancers. If successful, any cancers that are not supposed to be cured easily by radiation alone can now have a second chance. Side effects will be spared to major organs. Radiation in high doses will be delivered only to cancerous tumors.

For the argument that only renal cell carcinoma can be treated by the suggestion in the invention, it should be kindly reminded the FDG is located in nearly 90% of ALL common cancers with avidity and robust activity. Most cancers actually utilize more FDG and have higher SUV than renal cell carcinomas. Medicare of the United States has now approved usage of FDG for PET scanning in tumors like lung cancer, breast cancer, melanoma, lymphomas, colon cancer and head and neck cancer etc. Other common cancers are well under way to be included as standard care diagnosis eligible for Medicare reimbursements. As such, FDG is therefore proven to accumulate successfully in most common cancers. This invention will add the therapeutic approach of this molecule to all these cancers. The applicant hereby requests that practically all cancers be included into this invention, and not limited to renal cell cancer.

In conclusion, the applicant hope to address the removal of 112 rejections for claims 3-6 by the full description of the invention process, the direction and guidance presented with specification to cancer and working examples. The level of skill of those in the art for this invention and unpredictability is quite low compared to the amount of skill and experience required by a medical oncologist or radiotherapist to receive their proper license to practice requirements. Prior art such as the use of radioactive iodine for thyroid cancer has well been published and used on a daily basis by similar practitioners. There is also a very low demand for experimentation needed for the invention since FDG has been used worldwide and approved by the FDA, with essentially no adverse side effects for many years. All that is needed as mentioned above, is for the practitioner of the art to request the material from local cyclotron centers. Submission of a protocol to the internal review board of the hospital that he/she is

experimental. This process, however, will not require a high level of technical skill or experimentation.

Thank you for your kind consideration.

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Respectfully submitted

By: 

YEUNG, Alex Wah Hin, Dr.
Inventor
C/O
Plasmagene Biosciences Ltd.
5th floor Club Lusitano Building
16 Ice House Street
Central
Hong Kong
Office Phone: 852-2948-9898
Office Fax: 852-2948-9899
Email: alex.yeung@plasma-gene.com